From the:
INTERNATIONAL SEARCHING AUTHORITY

To:

Griffith Hack
GPO Box 4164
SYDNEY NSW 2001

-

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)*	04 MAY 2005
Applicant's or agent's file reference SDS:BR:FP21285	FOR FURTHER ACTION See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/AU2005/000442	30 March 2005	30 March 2004

International Patent Classification (IPC) or both national classification and IPC
Int. Cl.[7] A61K 31/19; A61P 29/02

Applicant
THE UNIVERSITY OF SYDNEY et al

1. This opinion contains indications relating to the following items:

- [X] Box No. I Basis of the opinion
- [ ] Box No. II Priority
- [ ] Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- [ ] Box No. IV Lack of unity of invention
- [X] Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- [ ] Box No. VI Certain documents cited
- [ ] Box No. VII Certain defects in the international application
- [X] Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the IPEA/AU	Authorized Officer
AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	MICHIYO MATSUDA Telephone No. (02) 6283 2502

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/AU2005/000442

Box No. I Basis of the opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material

      ☐ a sequence listing
      ☐ table(s) related to the sequence listing

   b. format of material

      ☐ in written format
      ☐ in computer readable form

   c. time of filing/furnishing

      ☐ contained in the international application as filed.
      ☐ filed together with the international application in computer readable form.
      ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/AU2005/000442

Box No. V **Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims 1-29	YES
	Claims	NO
Inventive step (IS)	Claims	YES
	Claims 1-29	NO
Industrial applicability (IA)	Claims 1-29	YES
	Claims	NO

2. Citations and explanations:

D1. WO 2004/000215 A2 (Medinox Inc) 31 December 2003

D2. Roch-Arveiller M et al "Effects of some non-steroidal anti-inflammatory drug copper complexes on polymorphonuclear leukocyte oxidative metabolism" Agents and Actions (1990) Vol 31 (1-2) pages 65-71

D3. Roch-Arveiller M et al "Non-steroidal anti-inflammatory drug-copper complex modulation of polymorphonuclear leukocyte migration" Biochemical Pharmacology (1990) Vol 39(3) pages 569-74

D4. West GB "Testing for drugs inhibiting the formation of gastric ulcers" Journal of Pharmacological Methods (1982) Vol 8(1) pages 33-7

Novelty (N)
Claims 1-29 meet the criteria set forth in PCT Article 33(2) for novelty. D1 discloses a hydroxamate complex of NSAIDs in an emulsion, dispersion, or a micelle. D2 discloses metal complexes of NSAIDs. D3 discloses metal complexes of NSAIDs suspended in water soluble methyl cellulose. D4 discloses copper salicylate in water soluble Tween 80. The prior art published before the priority date therefore, does not independently disclose a composition comprising a metal complex of a carboxylate having anti-inflammatory activity, wherein the composition has a colloidal structure, or forms a colloidal structure, or is immiscible with water.

Inventive Step (IS)

As indicated in D1 and also in the current invention, NSAIDs are known to cause adverse side effects, such as gastrointestinal ulceration. D1 overcomes this problem by providing a hydroxamate complex of NSAIDs, in the form of an emulsion, dispersion, or a micelle. As described in the current application (at page 2), metal complexes of NSAIDs are known in the art to have less side effects than free NSAID and as disclosed in D2, are more effective than the free NSAIDs in providing anti-inflammatory activity. It is common general knowledge in the art to formulate pharmaceutical compositions as an emulsion, dispersion, or a micelle such as in D1. It is therefore considered that it would be obvious to a person skilled in the art to formulate a metal complex of NSAIDs as disclosed in D2 in the form of an emulsion, dispersion, or micelle as in the current invention.

The claimed invention is not obvious in light of D3 and D4 which disclose compositions containing metal complexes of NSAIDs with water soluble compounds.

Industrial Applicability (IA)

The invention defined in claims 1-29 is industrially applicable

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/AU2005/000442

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claims 1-8, 10-29 are not fully supported by the description which only provides support for selected metal complexes of a carboxylate having anti-inflammatory activity.